IMPROVED INFARCT ARTERY PATENCY USING A NEW MODIFIED REGIMEN OF t-PA: RESULTS OF THE PRE-HOSPITAL ADMINISTRATION OF t-PA (PATS) PILOT TRIAL.

George R. McKendall, M.D., Michael Attubato, M.D., Thomas M. Drew, M.D., F.A.C.C., Frederick Feit, M.D., F.A.C.C., Barry Sharaf, M.D., Edward S. Thomas, M.D., Mary Jane McDonald, R. N., David O. Williams, M.D., F.A.C.C., Rhode Island Hospital, Brown University, Providence, RI and Bellevue Hospital, New York University, New York, NY.

The efficacy and safety of a new dosing regimen of intravenous (IV) t-PA for acute myocardial infarction (AMI) was determined in an open label angiographic study. Thirty-six consecutive eligible patients who presented to the hospital with AMI were given a 20 mg. IV bolus of t-PA followed 30 minutes later by an infusion of 80 mg. over two hours, a regimen tailored to potential pre-hospital paramedic administration. The primary end point was 90 minute infarct related artery (IRA) patency (TIMI II or III flow), determined by acute coronary angiography. Secondary end points included clinical events such as death, bleeding, and in-hospital recurrent ischemia. Patency rates at 30, 60, 90 and 120 minutes following t-PA initiation are shown below.

	Elapsed Time After Bolus/Infusion (min.)			
	30	60	90	120
n (patients)	13	34	36	34
IRA: % Patent	38.5%	82.4%	94.4%	94.1%
Cumulative Dose (mg.)	20	53	80	90

The 90 minute patency rate was 94.4%. Only two patients (5.5%) required a blood transfusion, both related to bleeding at catheterization site. Seventeen patients (47.2%) required predischarge revascularization for recurrent symptoms, provokable ischemia, or anatomical considerations. This included five patients (13.8%) who underwent acute PTCA at initial catheterization. These results demonstrate the improved efficacy of a new regimen of t-PA which features an initial 20 mg. bolus followed by a sustained infusion.

SYSTEMIC THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION WITH PROUROKINASE AND UROKINASE (STAMP): RESULTS OF A RANDOMIZED MULTICENTER STUDY.

Karl R. Karsch, M.D., Georg Ertl, M.D., Bernd Kunkel, M.D. and the STAMP study group,
University of Tuebingen, Medical Clinic, FRG

The purpose of the study was to determine the efficacy of iv.thrombolysis using a combination of Prourokinase (PUK 4,5 Mio.IE) and Urokinase (UK 250 000 IE) in comparison to i.v. Streptokinase therapy (SK 1,5 Mio.IE). 219 pts. with acute myocardial infarction of less than 6 hours were enrolled in the prospective multicenter randomized trial. The primary endpoint was patency of the infarct vessel at angiography 14 days after thrombolysis and in-hospital mortality. Non-invasive signs of reperfusion were derived from serial CK- and CKMB determination. In-hospital mortality was comparable in both groups. Early reperfusion rate (<12 hrs)was significantly ($p<0.001$) higher in the SK group. Late patency was 82% for the SK and 63% for the PUK+UK group ($p<0.01$). Bleeding complications were significantly reduced in the PUK+UK group (SK:20%; PUK+UK:4.3%; $p<0.01$).

Thus, the combination of PUK+UK, at the doses employed, resulted in a reduced rate of reperfusion and late patency compared to SK.

A SYSTEMIC NON-LYTIC STATE PREDICTS FAILURE OF ANISOYLATED PLASMINOGEN STREPTOKINASE ACTIVATING COMPLEX (APSAC) IN ACUTE MYOCARDIAL INFARCTION.

Johan Brügemann, M.D., Bert H. Takens M.D., Jan van der Meer M.D., Kong I. Lie M.D., Ph.D., Thoraxcentre, University Hospital Groningen, The Netherlands.

In 58 patients (age 34-71, mean 57 years) with acute myocardial infarction APSAC 30 U i.v. was administered within 4 hours after onset of symptoms. Infusion with heparin was started 1-4 hours after APSAC in a dosage of 30.000 U/24 hours. Blood samples for coagulation parameters were taken serially. Decrease of the fibrinogen level to below 1.0 g/l within 1.5 hours after administration of APSAC was considered to reflect a systemic lytic state. Coronary angiography was performed 1.5 and 48 hours after thrombolytic treatment in 30 and 58 patients respectively.

	lytic state			non-lytic state			
	0	1.5	48	0	1.5	48	(hours)
fibrinogen	3.1	0.0	2.5	2.9	2.3	4.2	(g/l)
plasminogen	97	11	55	104	57	78	(%)
antiplasmin	93	4	80	90	35	99	(%)
patency		43			0		
non-patency		9			6		

The overall achieved patency rate was 74% (43/58). Patency rates were 83% (43/52) and 0% (0/6) in patients with a lytic and a non-lytic state respectively. Fisher's exact test indicates this to be a significant relation with $p<0.001$.

We conclude that the absence of a systemic lytic state after APSAC administration is highly predictive for failure of coronary thrombolysis.

ON THE COMBINED ADMINISTRATION OF SARUPLASE AND ALTEPLASE AND BOLUS ADMINISTRATION OF ALTEPLASE.

Bernardino Tranchesi*, Giovanni Bellotti*, Dalton F. Chamone*, Frans Van de Werf**, Philippe Vanhove***, Marc Verstraete***. *Hospital das Clinicas, São Paulo, Brasil; **Dept. of Cardiology and ***Ctr. Thrombosis & Vasc. Res., Leuven, Belgium.

Coronary recanalization of alteplase (20 mg) combined with 10 mg (Group A), 15 mg (Group B) or 20 mg (Group C) saruplase, administered intravenously (IV) over 90 min, was investigated in a double-blind trial in 43 patients with MI of < 5 hrs duration. Only patients with TIMI grades 0 or 1 of the IRA were selected and given IV heparin (1,000 U) and IC nitroglycerin (200 µg). Angiograms were evaluated by "blinded" experts.

	Group A	Group B	Group C
Recanalization at 90 min	4/14 (28%)	7/17 (41%)	4/12 (33%)
Immediate PTCA performed	78.6%	70.6%	72.7%
Fibrinogen (mg%) before	246 ± 50	254 ± 54	296 ± 90
at 90 min	250 ± 57	246 ± 60	256 ± 50

Thus, these drug combinations do not result in a satisfactory recanalization at the end of infusion.

A bolus dose of 70 mg alteplase was tested in 25 patients with MI, TIMI grade 0. A second bolus dose of 20 mg alteplase was only administered if the recanalization was < TIMI grade 3 at 60 min. The final coronary angiogram was made at 90 min.

Recanalization at 90 min	30 min	60 min	90 min
(TIMI 2-3) in all	13/25	18/25	18/25
25 patients	52%	72%	72%
Pts. receiving single	11/15	15/15	14/15
bolus only (N 15)	73%	100%	93%
Pts. receiving 2nd (20 mg)	2/10	3/10	4/10
bolus at 60 mg (N 10)	20%	30%	40%

Thus, 70 mg alteplase bolus results in a rapid and high recanalization rate. Whether this is the lowest effective bolus dose of alteplase is being investigated.